Rate Equation Approaches to Amplification of Enantiomeric Excess and Chiral Symmetry Breaking

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Abstract

Theoretical models and rate equations relevant to the Soai reaction are reviewed. It is found that in a production of chiral molecules from an achiral substrate autocatalytic processes can induce either enantiomeric excess (ee) amplification or chiral symmetry breaking. Former terminology means that the final ee value is larger than the initial value but depends on this, whereas the latter means the selection of a unique value of the final ee, independent of the initial value. The ee amplification takes place in an irreversible reaction such that all the substrate molecules are converted to chiral products and the reaction comes to a halt. The chiral symmetry breaking is possible when recycling processes are incorporated. Reactions become reversible and the system relaxes slowly to a unique final state. The difference between the two behaviors is apparent in the flow diagram in the phase space of chiral molecule concentrations. The ee amplification takes place when the flow terminates on a line of fixed points (or a fixed line), whereas symmetry breaking corresponds to the dissolution of the fixed line accompanied by the appearance of fixed points. Relevance of the Soai reaction to the homochirality in life is also discussed.

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I. INTRODUCTION

In the Human Genome Project (from the year 1990 to 2003) sequences of chemical base pairs that make up human DNA were intensively analyzed and determined, as it carries important genetic information. DNA is a polymer made up of a large number of deoxyribonucleotides, each of which composed of a nitrogenous base, a sugar and one or more phosphate groups [1]. Similar ribonucleotides polymerize to form RNA, which is also an important substance to produce a template for protein synthesis. RNA sometimes carries genetic information but rarely shows enzymatic functions [1].

One big issue of the post Genome Project is the proteomics since proteins play crucial roles in virtually all biological processes such as enzymatic catalysis, coordinated motion, mechanical support, etc. [1]. A protein is a long polymer of amino acids, and folds into regular structures to show its biological function.

Sugars and amino acids in these biological polymers contain carbon atoms, each of which is connected to four different groups, and consequently is able to take two kinds of stereostructures. The two stereoisomers are mirror images or enantiomers of each other, and are called the D- and L-isomers. Two isomers should have the same physical properties except optical responses to polarized light. Therefore, a simple symmetry argument leads to the conclusion that there are equal amount of D- and L-amino acids or sugars in life. But the standard biochemical textbook [1] tells us that "only L-amino acids are constituents of proteins" ([1], p.17), and "nearly all naturally occurring sugars belong to the D-series" ([1], p.346). There is no explanation why the chiral symmetry is broken in life and how the homochirality has been brought about on earth.

It is Pasteur who first recognized the chiral symmetry breaking in life in the middle of the 19th century. By crystallizing optically inactive sodium anmonium racemates, he separated two enantiomers of sodium ammonium tartrates with opposite optical activities by means of their asymmetric crystalline shapes [2]. Since the activity is observed even in the solution, it is concluded that the optical activity is due to the molecular asymmetry or chirality, not due to the crystalline symmetry. Because two enantiomers with different chiralities are identical in every chemical and physical properties except the optical activity, "artificial products have no molecular asymmetry" and in 1860 Pasteur stated that "the molecular asymmetry of natural organic products" establishes "the only well-marked line of demarcation that

can at present be drawn between the chemistry of dead matter and the chemistry of living matter" [3]. Also by using the fact that asymmetric chemical agents react differently with two types of enantiomers, he separated enantiomers by fermentation. Therefore, once one has an asymmetric substance, further separation of two enantiomers or even a production of a single type of enantiomer may follow [4]. But how has the first asymmetric organic compound been chosen in a prebiotic world?

This problem of the origin of homochirality in life has attracted attensions of many scientists in relation to the origin of life itself since the discovery of Pasteur [3, 5, 6, 7]. Japp expected a "directive force" when "life first arose" [3], and various "directive forces" are proposed later such as different intensities of circularly polarized light in a primordial era, adsorption on optically active crystals, or the parity breaking in the weak interaction. However, the expected degree of chiral asymmetry or the value of the enantiomeric excess (ee) turns out to be very small [6], and one needs a mechanism to amplify ee enormously to a level of homochirality.

Another scenario for the origin of homochirality was suggested by Pearson [8] such that the chance breaks the chiral symmetry. Though the mean number of right- and left-handed enantiomers are the same, there is nonzero probability of deviation from the equal populations of both enantiomers. The probability to establish homochirality in a macroscopic system is, of course, very small [9], but "chance produces a slight majority of one type of" enantiomers and "asymmetric compounds when they have once arisen" act as "breeders, with a power of selecting of their own kind of asymmetry form" [8]. In this scenario, produced enantiomer acts as a chiral catalyst for the production of its own kind and hence this process should be autocatalytic.

Nearly a century later, a long sought autocatalytic system with spontaneous amplification of chiral asymmetry is found by Soai and his coworkers [10]: In a closed reactor with achiral substrates addition of a small amount of chiral products with a slight enantiomeric imbalance yields the final products with an overwhelmingly amplified ee [10]. The autocatalytic system also shows significant ee amplification under a variety of organic and inorganic chiral initiators with a small enantiomeric imbalance [11]. When many reaction runs are performed without chiral additives, about half of the runs end up with the majority of one enantiomer, and the other half end up with the opposite enantiomer. The probability distribution of the ee is bimodal with double peaks, showing amplification of ee and further indicating the

occurrence of chiral symmetry breaking [12, 13, 14].

As for the theoretical research on the chiral symmetry breaking, Frank is the first to show that a linear autocatalysis with an antagonistic nonlinear chemical reaction can lead to homochirality [15]. His formulation with rate equations corresponds to the mean-field analysis of the phase transition in nonequilibrium situation [16], and other variants have been proposed [6, 17, 18, 19, 20, 21, 22]. All these analyses are carried out for open systems where the concentration of an achiral substrate is kept constant. Asymptotically the system approaches a unique steady state [6, 17, 18, 19, 20] or even an oscilatory state [21, 22], independent of the initial condition. When the final state is chirally asymmetric, one may call this a chiral symmetry breaking in the sense of statistical mechanics, and it is indicated in the right upper corner in Table 1. On the other hand, the Soai reaction is performed in a closed system and an achiral substrate is converted to chiral products irreversibly: The substrate concentration decreases in time, and eventually the reaction comes to a halt. After the reaction the ee value increases but its final value is found to depend on the initial state. Even though the ee is amplified, the history dependent behavior is different from what we expect from phase transitions in statistical mechanics, so that we write down "ee amplification" in the left lower corner in Table 1. We have analyzed theoretically the chiral symmetry breaking in a closed system in general, and found that with an irreversible nonlinear autocatalysis the system may show ee amplification as in the Soai reaction. Furthermore, with an additional recycling back reaction, a unique final state with a finite ee value is found possible, which we call a chiral symmetry breaking as is shown in the right lower corner in Table 1 [23, 24, 25, 26, 27, 28]. There are also many theoretical works on the Soai reaction in a closed system [29, 30, 31, 32, 33, 34, 35]. Here we give a brief survey of various theoretical models of the ee amplification and the chiral symmetry breaking in a closed system, though it is by no means exhaustive.

II. AMPLIFICATION IN MONOMERIC SYSTEMS

Two stereostructural isomers are called D- and L-enantiomers for sugars and amino acids, but, for general organic compounds, R and S representation is in common. We adopt $R - S$ representation hereafter.

We consider a production of chiral enantiomers R and S from an achiral substrate A in a

TABLE I: The ee amplification and the chiral symmetry breaking in an open and a closed system.

		Initial Condition	
		Dependent	Independent
System	Open		Chiral Symmetry Breaking
	Closed	ee Amplification	Chiral Symmetry Breaking

closed system. Actually, in the Soai reaction, chiral molecules are produced by the reaction of two achiral reactants A and B as $A + B \rightarrow R$ or $A + B \rightarrow S$. But in a closed system a substrate of smaller amount controls the reaction, since it is first consumed up and holds the reaction to proceed further. Therefore, in order to grasp main features of chirality selection, it is sufficient to assume that an achiral substrate A of a smaller amount converts to R or S. The process may further involve formation of intermediate complexes, oligomers etc., but for the purpose to discuss about relations and difference between the amplification and the symmetry breaking in chirality, we restrict our consideration in this section to the simplest case where only monomers are involved.

A. Reaction Schemes

The spontaneous production of chiral molecules R or S from an achiral substrate A is described by reactions

$$A \xrightarrow{k_0} R, \qquad A \xrightarrow{k_0} S. \tag{1}$$

We assume the same reaction rate k_0 for the nonautocatalytic spontaneous production of R and S enantiomers, since both of them are identical in every chemical and physical aspects: No advantage factor [6] is assumed.

Since the spontaneous production (1) yields only a racemic mixture of two enantiomers, one has to assume some autocatalytic processes. The simplest is a linear autocatalysis with

a reaction coefficient k_1 as

$$A + R \xrightarrow{k_1} 2R, \qquad A + S \xrightarrow{k_1} 2S. \tag{2}$$

There may be a linear cross catalytic reaction or erroneous linear catalysis with a coefficient k_1' as

$$A + R \xrightarrow{k_1'} S + R, \qquad A + S \xrightarrow{k_1'} R + S. \tag{3}$$
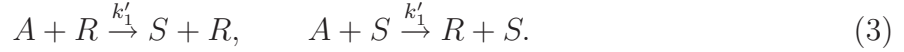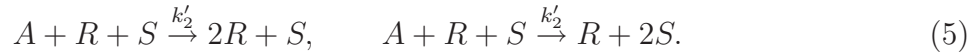
As will be discussed later, the linear autocatalysis alone is insufficient not only to break the chiral symmetry but also to amplify ee.

Beyond these linear autocatalyses, nonlinear effects such as quadratic autocatalysis have been considered as [6, 23, 30];

$$A + 2R \xrightarrow{k_2} 3R, \qquad A + 2S \xrightarrow{k_2} 3S, \tag{4}$$
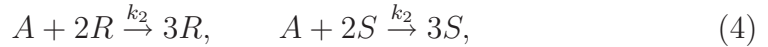
and cross catalysis as

$$A + R + S \xrightarrow{k_2'} 2R + S, \qquad A + R + S \xrightarrow{k_2'} R + 2S. \tag{5}$$

These higher order autocatalytic processes may actually be brought about by the dimer catalysts [18], but we confine ourselves to the simplest description (4) and (5) in terms of only monomers R and S in this section. Consideration on dimers is postponed in the following sections. The reaction (4) alone can give rise to the amplification of chirality as will be discussed. One notes that all these processes (1) to (5) unidirectionally produce chiral enantiomers and thus the reaction comes to a halt when the whole achiral substrate is consumed; the total process is irreversible.

B.   Rate equations and an order parameter

Concentrations r and s of two enantiomers R and S vary according to the reaction processes described in the previous subsection. In an open system, the achiral substrate is steadily supplied in such a way that its concentration a is kept constant. On the contrary, in a closed system, achiral substrates are transformed to chiral products and only the total concentration $c = a + r + s$ of reactive chemical species is kept constant. By denoting the total concentration of monomeric chiral products with a subscript 1 as

$$q_1 = r + s, \tag{6}$$

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the concentration of the substrate a is determined as

$$a = c - q_1, \qquad (7)$$

which should be non-negative. Then, the development of reactions in a closed system can be depicted as a flow in the triangular region in the r-s phase space

$$0 \le r, s, r + s \le c. \qquad (8)$$

The reaction schemes (1) to (5) induce rate equations for r and s as;

$$\frac{dr}{dt} = [f(r) + k_1's + k_2'rs]a$$
$$\frac{ds}{dt} = [f(s) + k_1'r + k_2'rs]a \qquad (9)$$

with an effective rate coefficient

$$f(r) = k_0 + k_1 r + k_2 r^2. \qquad (10)$$

Since the right-hand side of Eq.(9) for velocities $\dot{r} = dr/dt$ and $\dot{s} = ds/dt$ are always non-negative and in proportion to the concentration of the achiral substrate a, both r and s never decrease and stop to grow after a vanishes $(a = 0)$.

The asymptotic behavior of a two-dimensional autonomous dynamical system is, in general, known to have fixed points or lines where $\dot{r} = \dot{s} = 0$ or to have limit cycles where $\dot{r}, \dot{s} \neq 0$. Since the system is irreversible as the concentrations of chiral products always increase at the cost of the substrate A as

$$\frac{da}{dt} = -[f(r) + f(s) + k_1'(r + s) + 2k_2'rs]a \le 0 \qquad (11)$$

and no epimerization process $R \leftrightarrow S$ is assumed, limit cycle is impossible: Production stops when all the substrate molecules are transformed to chiral ones; $a(t = \infty) = 0$. Since $\dot{r} = \dot{s} = 0$ for $a = 0 = c - r - s$, the diagonal line $r + s = c$ is a fixed line for this irreversible system. Any points on the fixed line are marginally stable because they have no guaranteed stability along the fixed line.

Our interest is the dynamical behavior of ee or the chiral symmetry breaking and, in particular, as to whether ee increases asymptotically. In order to quantify the monomeric ee or the degree of chiral symmetry breaking, we define a monomeric order parameter ϕ_1 as

$$\phi_1 = \frac{r - s}{r + s} = \frac{r - s}{q_1}, \qquad (12)$$

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which is zero for a symmetric or racemic state ($r = s$), and is nonzero for a symmetry-broken or chiral state. The evolution equation of ϕ_1 is immediately derived from Eq.(9) as

$$\frac{d\phi_1}{dt} = A\phi_1 - B\phi_1^3 \tag{13}$$

with coefficients

$$A(t) = -2\frac{a}{q_1}(k_0 + k_1'q_1) + B(t),$$
$$B(t) = \frac{1}{2}(k_2 - k_2')q_1 a. \tag{14}$$

However, as $a(t = \infty) = 0$, both the coefficients A and B vanish asymptotically, and one cannot determine the final value of ee from the evolution equation (13). On a fixed line $r + s = c$ the ee value varies from $\phi_1 = -1$ at a point $(r, s) = (0, c)$ to $\phi_1 = 1$ at (c,0), and the final values of ϕ_1 can be anything between $+1$ and -1. In order to obtain the final value of ee, one has to solve the evolution (9) and especially to determine the trajectory of the dynamical flow in $r - s$ phase space.

C.   Flow Trajectory in a $r - s$ Phase Space

As the first step to analyze flow trajectories in a phase space, we consider the simplest case when reactions such as spontaneous production (1), linearly autocatalytic (2) or quadratically autocatalytic (4) reactions are active, respectively. Then the rate equations are simplified as

$$\frac{dr}{dt} = f(r)a,$$
$$\frac{ds}{dt} = f(s)a, \tag{15}$$

with the rate coefficient f defined in Eq.(10). Flow trajectories are obtained by integrating a trajectory equation

$$\frac{ds}{dr} = \frac{f(s)}{f(r)}. \tag{16}$$

In the following, an initial condition is set as $r = r_0$, $s = s_0$, $a_0 = c - r_0 - s_0$ (or $q = q_{1,0} = r_0 + s_0$, $\phi_1 = \phi_{1,0} = (r_0 - s_0)/q_{1,0}$, $a_0 = c - q_{1,0}$), and we discuss how the final ee value $\phi_{1,\infty}$ depends on the initial value $\phi_{1,0}$ for a few typical cases.
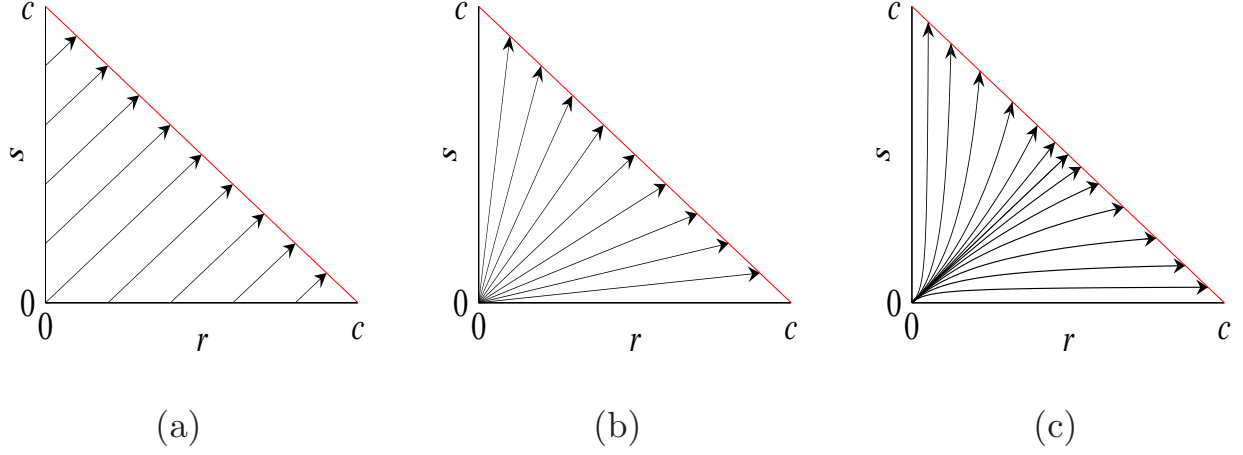
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FIG. 1: Flow diagrams for (a) spontaneous production ($k_0 > 0$, $k_1 = k_2 = 0$), (b) linearly autocatalytic ($k_1 > 0$, $k_0 = k_2 = 0$), and (c) quadratically autocatalytic ($k_2 > 0$, $k_0 = k_1 = 0$) reactions.

1. Spontaneous Production

When chiral molecules are produced only spontaneously and the system has no autocatalytic processes ($k_0 > 0$, $k_1 = k_2 = 0$), the trajectory in the $r - s$ phase space is obtained as

$$r - s = r_0 - s_0 = \text{const.} \tag{17}$$

The flow diagram is a straight line with a unit slope, terminating at the fixed line $r + s = c$, as shown in Fig.1(a). Half of the substrate a_0 initially present convert to R and the remaining half to S, and the ee decreases to the value $\phi_{1,\infty} = (q_{1,0}/c)\phi_{1,0}$. The smaller the ratio $q_{1,0}/c$ of the initial amount of chiral species to the total amount of active reactants is, the more the ee decreases, as shown in Fig.2(a).

2. Linear Autocatalysis

When only the linearly autocatalytic production of chiral molecules is active ($k_1 > 0$, $k_0 = k_2 = 0$), the trajectory is obtained as

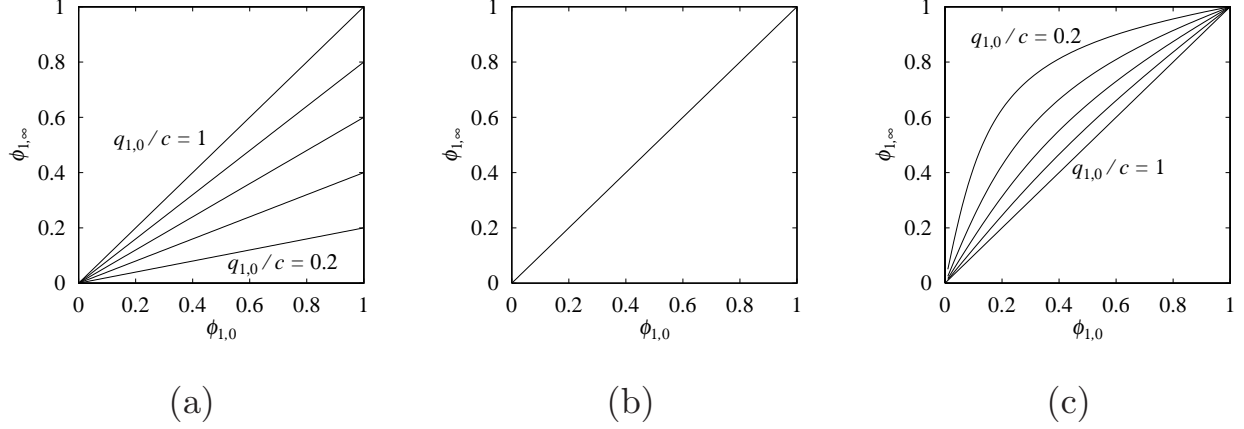$$\frac{s}{r} = \frac{s_0}{r_0} = \text{const.} \tag{18}$$

FIG. 2: The final ee $\phi_{1,\infty}$ versus the initial ee $\phi_{1,0}$ for (a) spontaneous production ($k_0 > 0$, $k_1 = k_2 = 0$), (b) linearly autocatalytic ($k_1 > 0$, $k_0 = k_2 = 0$), and (c) quadratically autocatalytic ($k_2 > 0$, $k_0 = k_1 = 0$) reactions. Each curve corresponds to a fixed ratio of the initial amount of chiral species to the total amount of active reactants $q_{1,0}/c$. As the ratio decreases, the initial slope of the curve decreases in (a), does not change in (b), and increases in (c).

and the flow diagram is a straight line radiating from the origin and terminating at the fixed line $r + s = c$, as shown in Fig.1(b). The ee value remains constant as

$$\phi_{1,\infty} = \phi_{1,0} = \text{const.} \tag{19}$$

and is independent of the initial ratio $q_{1,0}/c$, as shown in Fig.2(b).

If the erroneous linear catalysis (3) is at work in addition to the linear autocatalysis (2), rate equations are modified as

$$\frac{dr}{dt} = (k_1 r + k_1' s)a,$$
$$\frac{ds}{dt} = (k_1 s + k_1' r)a. \tag{20}$$

These equations can be combined to yield

$$\frac{d\phi_1}{dq_1} = -(1 - f)\frac{\phi_1}{q_1}, \tag{21}$$

with a fidelity factor f defined by

$$f = \frac{k_1 - k_1'}{k_1 + k_1'} \tag{22}$$

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which is unity without the error $k_1' = 0$ and vanishes when $k_1 = k_1'$. The ee value ϕ_1 is easily integrated as

$$\phi_{1,\infty} = \phi_{1,0}\left(\frac{q_{1,0}}{c}\right)^{1-f} \leq \phi_{1,0}. \tag{23}$$

This result shows that the final value is less than the initial $\phi_{1,0}$ whenever there is a finite error process $f < 1$. In particular, if $f = 0$, the final ee behaves the same with that of the spontaneous production.

3.   Quadratic Autocatalysis

With only a quadratic autocatalysis ($k_2 > 0,\ k_0 = k_1 = 0$), the trajectory is obtained as

$$\frac{1}{r} - \frac{1}{s} = \frac{1}{r_0} - \frac{1}{s_0} = \text{const.} \tag{24}$$

and the flow diagram is hyperbolae radiating out from the origin and terminating at the fixed line $r + s = c$, as shown in Fig.1(c). Below the diagonal $r = s$ line, the flow bents downward and the ratio s/r decreases as time passes, and consequently the ee value ϕ_1 increases. In other words, by using the relation $r = q_1(1 + \phi_1)/2$ and $s = q_1(1 - \phi_1)/2$, the ee value is easily found from Eq.(24) to satisfy a relation

$$\frac{\phi_1}{1 - \phi_1^2} = Aq_1 \tag{25}$$

with a constant A determined by an initial condition. For a given value of q_1, the ee value ϕ_1 is determined graphically as a cross point of two curves representing both sides of Eq.(25), as shown in Fig.3. Then, it is evident that ϕ_1 increases as q_1 increases. The asymptotic value corresponding to $q_1 = c$ is obtained as

$$\phi_{1,\infty} = \frac{1}{2cA}\left[\sqrt{1 + (2cA)^2} - 1\right] \tag{26}$$

The relation between the initial value $\phi_{1,0}$ of the ee and its final value $\phi_{1,\infty}$ is depicted in Fig.2(c) for fixed values of the initial amount $q_{1,0}$ of chiral species relative to the total amount c. The smaller the initial ratio $q_{1,0}/c$, the more prominent the ee amplification.

The ee amplification curves possess a remarkable property such that they depend on the initial ratio $q_{1,0}/c$ but are independent of the rate coefficient k_2. The latter determines the time evolution of ϕ_1 but not its final value. If there are other processes involved, for instance
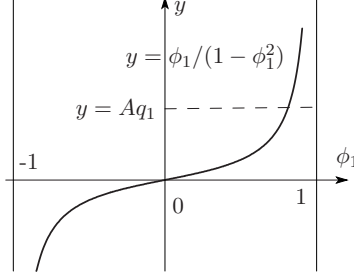
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FIG. 3: The ee value ϕ_1 is given at a cross point with two curves, $y = \phi_1/(1 - \phi_1^2)$ and $y = Aq_1$.

the spontaneous production $k_0 \neq 0$, then amplification curves should depend on the ratio $k_0/k_2 c^2$.

If there is a racemizing cross catalysis (5) with k_2', the trajectory equation is rewritten as

$$\frac{d\phi_1}{dq_1} = \frac{\phi_1(1 - \phi_1^2)}{f_\times^{-1} + \phi_1^2} \frac{1}{q_1} \tag{27}$$

with a crossing effect factor defined by

$$f_\times = \frac{k_2 - k_2'}{k_2 + k_2'} \tag{28}$$

which is unity without a cross catalysis term ($k_2' = 0$) and vanishes when $k_2 = k_2'$. The solution of Eq.(27) is given by

$$\frac{\phi_1}{(1 - \phi_1^2)^{(1+f_\times)/2}} = Aq_1^{f_\times}. \tag{29}$$

From this result one can see that the asymptotic value $\phi_{1,\infty}$ decreases as $f_\times$ decreases. In particular, when $f_\times = 0$, ϕ is independent of q_1 and does not vary; $\phi_{1,\infty} = \phi_{1,0}$. Namely, chirality amplification by k_2 is completely cancelled out by the racemization effect caused by k_2'.

III. AMPLIFICATION WITH HOMODIMER CATALYST

In order to understand molecular mechanisms how the quadratic autocatalysis is brought about, the concept of dimer catalyst introduced by Kagan and coworkers may be relevant [18, 29, 31, 32]. Assume that monomers R and S react to form homodimers R_2 and S_2 with a rate ν_{hom} and a heterodimer RS with a rate ν_{het}

$$R + R \overset{\nu_{\mathrm{hom}}}{\rightarrow} R_2, \qquad S + S \overset{\nu_{\mathrm{hom}}}{\rightarrow} S_2, \qquad R + S \overset{\nu_{\mathrm{het}}}{\rightarrow} RS. \tag{30}$$

Corresponding decomposition processes are described as

$$R_2 \overset{\nu'_{\text{hom}}}{\Rightarrow} R + R, \qquad S_2 \overset{\nu'_{\text{hom}}}{\Rightarrow} S + S, \qquad RS \overset{\nu'_{\text{het}}}{\Rightarrow} R + S. \tag{31}$$

Homodimers thus formed are assumed to catalyze of their own enantiomeric type as

$$A + R_2 \overset{k_{\text{hom}}}{\Rightarrow} R + R_2, \qquad A + S_2 \overset{k_{\text{hom}}}{\Rightarrow} S + S_2, \tag{32}$$
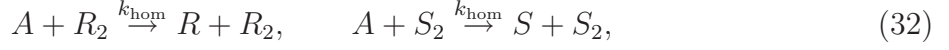
whereas heterodimers have no preference in enantioselectivity as

$$A + RS \overset{k_{\text{het}}}{\Rightarrow} R + RS, \qquad A + RS \overset{k_{\text{het}}}{\Rightarrow} S + RS \tag{33}$$
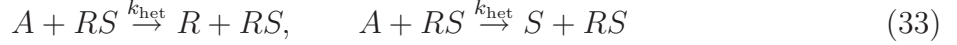
Now, the state of the system is described not only by the concentrations of monomers r and s, but also by those of dimers denoted as $[R_2]$, $[S_2]$ and $[RS]$ respectively. The rate equations are

$$\frac{dr}{dt} = k_0 a + k_{\text{hom}} a [R_2] - 2\nu_{\text{hom}} r^2 + 2\nu'_{\text{hom}}[R_2]$$
$$- \nu_{\text{het}} rs + \nu'_{\text{het}}[RS] + k_{\text{het}} a[RS],$$
$$\frac{d[R_2]}{dt} = \nu_{\text{hom}} r^2 - \nu'_{\text{hom}}[R_2],$$
$$\frac{d[RS]}{dt} = \nu_{\text{het}} rs - \nu'_{\text{het}}[RS], \tag{34}$$

and the corresponding ones for the S enantiomer. The ee or the chiral order parameter is now defined by

$$\phi = \frac{r + 2[R_2] - s - 2[S_2]}{q}. \tag{35}$$

where q is the total concentration of chiral molecules given as

$$q = r + s + 2[R_2] + 2[RS] + 2[S_2]. \tag{36}$$

If the dimerization and decomposition proceed very fast, the dimer concentrations take quasi-equilibrium values which satisfy $[\dot{R}_2] = [\dot{RS}] = [\dot{S}_2] = 0$ and are determined by the instantaneous monomer concentrations r and s as

$$[R_2] = \frac{\nu_{\text{hom}}}{\nu'_{\text{hom}}} r^2, \quad [RS] = \frac{\nu_{\text{het}}}{\nu'_{\text{het}}} rs, \quad [S_2] = \frac{\nu_{\text{hom}}}{\nu'_{\text{hom}}} s^2. \tag{37}$$

Then, the equations for monomers in Eq.(34) reduce to Eq.(9) with the coefficients k_2 and k'_2 given as

$$k_2 = k_{\text{hom}} \frac{\nu_{\text{hom}}}{\nu'_{\text{hom}}}, \quad k'_2 = k_{\text{het}} \frac{\nu_{\text{het}}}{\nu'_{\text{het}}} \tag{38}$$

and with $k_1 = k_1' = 0$.

As the reaction proceeds, the whole achiral substrate is ultimately transformed to chiral products so that $a = c - q_\infty = 0$. This represents a quadratic curve of fixed points in $r - s$ phase space. When there is solely a homodimer catalytic effect $k_2 > 0$ without spontaneous production nor heterodimer racemization $k_0 = k_2' = 0$, the initial state with (r_0, s_0) follows the hyperbolic flow trajectory (24) and ends up on the curve of fixed points, $q = c$, as shown in Fig.4(a).

The ratio r/s increases along the flow trajectory if it is initially larger than unity. Thus the $r - s$ asymmetry increases, and the final value of the ee $|\phi_\infty|$ is larger than the initial value $|\phi_0|$. Figure 4(b) shows $\phi_0 - \phi_\infty$ relation for cases of positive ϕ. The enhancement is more evident when the initial ratio q_0/c is smaller. These essential features are the same with the monomeric system.
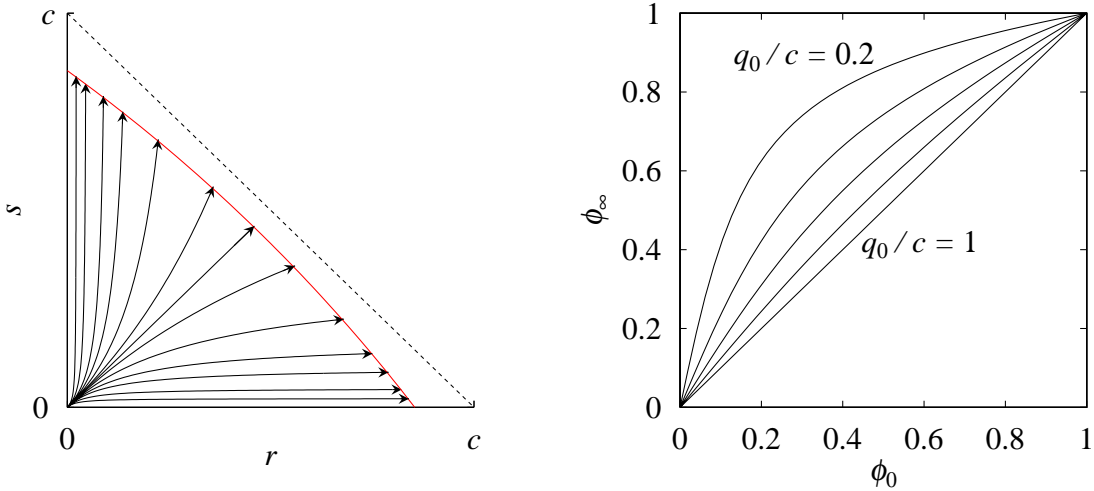

FIG. 4: (a) Flow diagrams for homodimer catalyst with $\nu_{\text{hom}}c/\nu_{\text{hom}}' = 0.1$ and $\nu_{\text{het}} = \nu_{\text{het}}' = 0$. Flow terminates on a curve of fixed points $q = c$. (b) The final ee value ϕ_∞ as a function of its initial value ϕ_0 for various amount of initial chiral species q_0. The less q_0 is, the more amplified ϕ_∞ is.

IV. AMPLIFICATION WITH ANTAGONISTIC HETERODIMER

Another model for the chiral asymmetry amplification is a variant of the Frank model in a closed system [33]. In its simplest form, the model consists of reaction schemes of a

spontaneous production (1), a linear autocatalysis (2) and a heterodimer formation (31). Then the rate equations for monomers are the same with those of the original Frank model [15], but they are supplemented with the heterodimer formation

$$\frac{dr}{dt} = k_0 a + k_1 ar - \nu_{\text{het}} rs,$$
$$\frac{ds}{dt} = k_0 a + k_1 as - \nu_{\text{het}} rs$$
$$\frac{d[RS]}{dt} = \nu_{\text{het}} rs \tag{39}$$

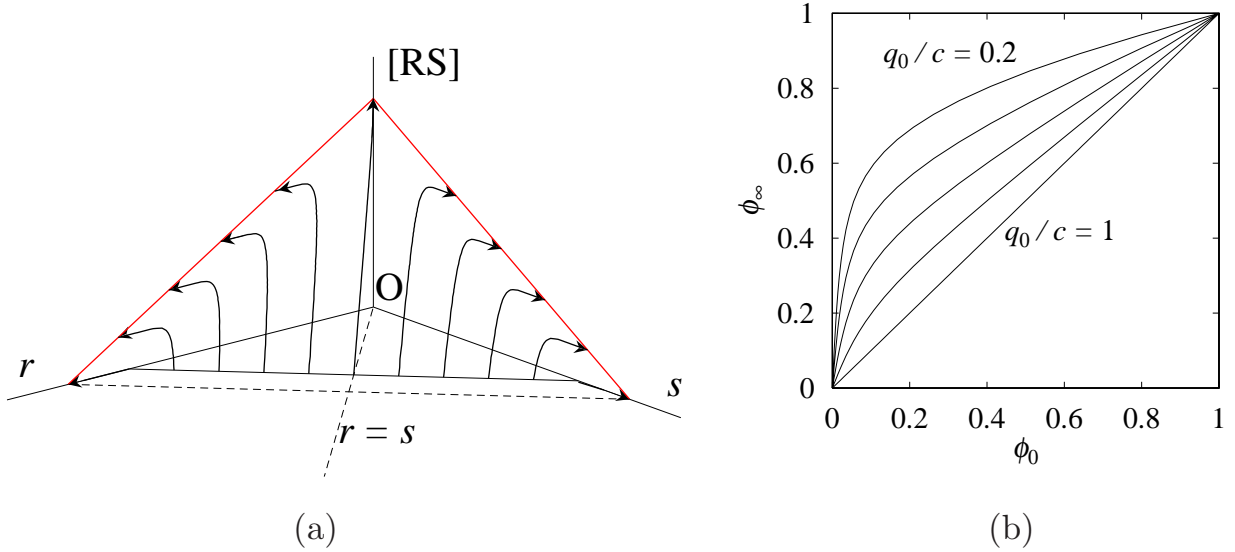
(a)   (b)

FIG. 5: (a) 3D flow diagrams for reactions with antagonistic heterodimers RS. Red lines represent fixed lines. Initial amount of achiral substrate is $0.2c$, and the remaining $q_0 = 0.8c$ is shared by R and S monomers. There are no heterodimers initially. Rate coefficients are $k_0 = 0$, $k_1 c = 1$, $\nu_{\text{het}} c = 10$. (b) Final ee ϕ_∞ versus its initial value ϕ_0 for a given initial ratio q_0/c. As q_0/c decreases, the ee amplification increases.

Since every achiral substrate is consumed up eventually $a(t = \infty) = 0$ and all the reactions stop asymptotically, Eq.(39) tells us that the product rs should vanish. If there is more R than S initially, S monomer disappears ultimately, for instance. But S molecules do not disappear nor decomposed back into achiral substrate. They are only incorporated into the heterodimer RS. The system is not determined solely by monomer concentrations r and s, (or ϕ_1 and q_1) but it depends on heterodimer concentration $[RS]$ as well. The flow takes place in a three-dimensional phase space of r, s, $[RS]$, as shown in Fig.5(a).

The asymptotics discussed above forces both the concentrations of the substrate $a = c - r - s - 2[RS]$ and the product rs vanish ultimately. These two conditions define a line of fixed points in the three-dimensional $r - s - [RS]$ phase space. If the initial state has a prejudice to R enantiomer such as $r_0 > s_0$, then the system ends up on a fixed line $r + 2[RS] = c$ on a $s = 0$ plane, as shown in Fig.5(a). Otherwise with $r_0 < s_0$, the system flows to another fixed line $s + 2[RS] = c$ on a $r = 0$ plane. The plane $r = s$ is a dividing surface that determines the final preference of chirality.

One can readily find that ee is amplified by the reaction involving antagonistic heterodimer, as shown in Fig.5(b). For a given amount of initial total concentration of chiral species $q_0 = r_0 + s_0$, the ee value ϕ increases by the completion of a reaction. No heterodimer is assumed to exist initially, $[RS]_0 = 0$. The amplification is more significant for smaller amount of q_0/c and ϕ_0. We note that the rate constant of heterodimerization ν_{het} has to be large in order to produce strong ee amplification. Minority enantiomer should be quickly incorporated into heterodimers before the achiral substrate is consumed up. Otherwise, both enantiomers consume up the achiral resource A and slowly forms heterodimers afterwards but without significant ee amplification. For a large ν_{het}, minority enentiomers are incorporated into heterodimers in an early stage. Therefore, flow trajectories first point upwards in Fig.5(a), indicating the rapid increase of heterodimer concentration $[RS]$. The trajectory is in fact inclined such that the minority enantiomer decreases its monomeric concentration. When it almost disappears, then the trajectory makes a quick turn in the vicinity of $r = 0$ plane or $s = 0$ plane, indicating the concentration growth of the surviving majority enantiomer.

V. RECYCLING AND FLOW: CHIRAL SYMMETRY BREAKING

So far, we have discussed several models for the ee amplification. There, the irreversibility of the dynamical system is essential to make the final state dependent on the initial condition. In this section, we consider the effect induced by introducing reversibility in the system by including various types of recycling processes. For simplicity, we consider in terms of a monomeric system.

In addition to the catalytic production processes (1) to (5), we include the recycling process such that enantiomeric products R or S undergo a back reaction to the substrate A
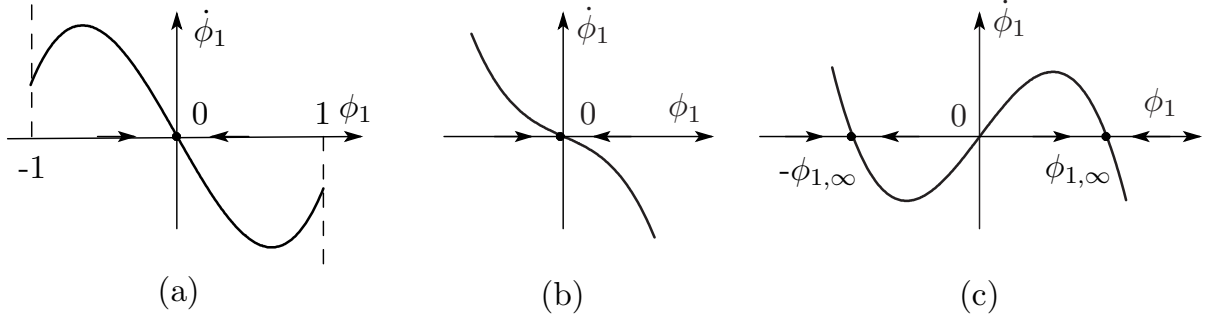
FIG. 6: ϕ_1 versus the velocity $\dot{\phi}_1 = A\phi_1 - B\phi_1^3$ for three typical cases: (a) $A < B < 0$, (b) $A < 0 < B$, and (c) $0 < A < B$.

[23] with a reaction rate λ as

$$R \xrightarrow{\lambda} A, \qquad S \xrightarrow{\lambda} A. \tag{40}$$

We call this reaction a linear recycling hereafter. One can also assume a nonlinear type of recycling process [27] such that different chiral species by their encounter react back to achiral molecules as

$$R + S \xrightarrow{\mu} 2A. \tag{41}$$

This back reaction can be a combined effect of the following two processes

$$R + S \xrightarrow{\mu} R + A$$
$$R + S \xrightarrow{\mu} S + A. \tag{42}$$

The rate equations now read as

$$\frac{dr}{dt} = [f(r) + k_1's + k_2'rs]a - \mu rs - \lambda r$$
$$\frac{ds}{dt} = [f(s) + k_1'r + k_2'rs]a - \mu rs - \lambda s. \tag{43}$$

The term with μ has a same form with the contribution of Frank's mutual inhibition [15]. The corresponding time-evolution of ϕ_1 is readily derived in the form of Eq.(13) with coefficients A and B determined by symmetric quantities q_1 and $a = c - q_1$ as

$$A(t) = -2\frac{a}{q_1}(k_0 + k_1'q_1) + B(t),$$
$$B(t) = \frac{1}{2}[(k_2 - k_2')a + \mu]q_1. \tag{44}$$

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The evolution Eq.(13) of the order parameter has a similar form with the time-dependent Landau equation [16] which is fundamental in nonequilibrium phase transitions. The asymptotic value of the order parameter $\phi_{1,\infty}$ is determined as the zero of the velocity $\dot{\phi}_1$. The main difference from the standard model of phase transitions lies in the time-dependence in the coefficients $A(t)$ and $B(t)$ induced by that of the achiral concentration $a(t)$ and the total chiral concentration $q_1(t)$. Because the concentrations a and q_1 are non-negative, $A(t)$ cannot exceed $B(t)$; $A(t) \leq B(t)$.

In previous sections we have focused our studies on the cases with $\lambda = \mu = 0$. In these cases, the asymptotic value of a vanishes, $a(t = \infty) = 0$ so that $A(t = \infty) = B(t = \infty) = 0$, and the asymptotic value of the order parameter ϕ_1 cannot be determined from Eq.(13). Another example with $A = B = 0$ happens for a special case with $k_0 = k'_1 = \mu = 0$ and $k_2 = k'_2$. In this case, we can calculate trajectories and find a fixed line shifted from $a = 0$ to the one with a finite value of $a(t = \infty)$ [27]: Flow trajectories are along lines passing through the origin, similar to those shown in Fig.1(b), but terminating at a shifted fixed line. Since $a = 0$ is no more a fixed line, trajectories not only point out from the origin, but also come out from the line $a = 0$.

In all the other cases, with either a linear or a nonlinear recycling process or with both, the coefficients A and B are no longer zero at the same time, and a definite value of the order parameter ϕ_1 is obtained asymptotically. The reason for the above is as follows. If the nonlinear recycling exists as $\mu > 0$, B becomes nonzero since $\mu q_{1,\infty} > 0$. If the linear recycling exists as $\lambda > 0$, not all the achiral substrate transform to chiral products but a finite amount remains asymptotically as $a(t = \infty) > 0$. Therefore, nonzero values of k_0, k'_1 or $k_2 \neq k'_2$ give contributions to the coefficients A or B.

For nonzero A and/or B, the velocity $\dot{\phi}_1 = d\phi_1/dt$ has three typical behaviors as a function of the order parameter ϕ_1, as shown in Fig.6. In the region with a positive (negative) velocity $\dot{\phi}_1$, ϕ_1 increases (decreases) and moves to the right (left), as indicated by arrows on the ϕ_1 axis in Fig.6. When A is negative, as in Fig.6(a) or (b), ϕ_1 eventually approaches the racemic value $\phi_1 = 0$ within its range of definition $|\phi_1| \leq 1$: The racemic state is a stable fixed point for $A < 0$. Equation (44) tells us that this happens when the spontaneous production k_0 or error in a linear autocatalytic process k'_1 are sufficiently strong, or quadratic catalysis k_2 is weaker than the cross catalysis k'_2. The coefficient of the linear autocatalysis k_1 as well as the linear recycling process λ are absent in the coefficients A and B, and cannot affect

directly the chirality of the system. These linear processes with k_1 and λ affect the chirality only implicitly through a and q_1.

When A is positive, as in the case of Fig.6(c), the coefficient of the cubic term B is also positive, and the velocity $\dot{\phi}$ vanishes at three values of ϕ_1 in the range of $-1 \le \phi_1 \le 1$. This is possible if a strong quadratic autocatalysis $k_2 > k_2'$ exists together with a linear recycling $\lambda > 0$, or if a linear autocatalysis k_1 and a nonlinear recycling $\mu > 0$ coexist. By following the direction indicated by the arrows for positive ϕ_1, the order parameter ends up at a definite value

$$\phi_{1,\infty} = \sqrt{\frac{A(t = \infty)}{B(t = \infty)}} \tag{45}$$

and the chiral symmetry breaking takes place. If the system starts with a negative ϕ_1, it stops at $-\phi_{1,\infty}$. The final state of the system depends on the initial sign of $\phi_{1,0}$, but independent of its magnitude $|\phi_{1,0}|$. We note that the asymptotic values of the coefficients $A(t = \infty)$ and $B(t = \infty)$ are independent of the initial condition and so is $|\phi_{1,\infty}|$. This situation is what we mean the "chiral symmetry breaking" in the sense of statistical mechanics.

We first discuss the chiral symmetry breaking when there is a nonlinear recycling, $\mu > 0$ [15, 27]. The rate Eq.(43) tells us that $a = c - r - s = 0$ is no more a fixed line, but we have many fixed points. The simplest is the case with only a linear autocatalysis $k_1 > 0$ but nothing else ($k_0 = k_1' = k_2 = k_2' = \lambda = 0$). In this case we have four fixed points in the $r - s$ phase space: two unstable ones, O and U, and two stable ones at $(r, s) = (c, 0)$ or $(0, c)$, as is shown in Fig.7(a). At the stable fixed points the final ee take values $\phi_{1,\infty} = \pm 1$. These values agree with those expected from Eq.(45) with $A(t) = B(t) = \mu q_1/2$ as determined from Eq.(44). The nonlinear recycling (42) returns the same amount of enantiomers back to the achiral substrate, but the relative decrement in concentration is larger for the minority enantiomer than for the majority one. The damage is further amplified by a large reduction of linear autocatalytic effect for the minority enantiomer, and it disappears at last.

As for the second example, we consider the case with a quadratic autocatalysis $k_2 > 0$ and a linear recycling $\lambda > 0$. Because the linear recycling takes place whenever there is nonzero concentrations of enantiomers, a few achiral substrate always remain, $a(t = \infty) \neq 0$. Thus the diagonal line $q_1 = r + s = c$ is no more a fixed line. Instead there appear fixed points in general. In the present case with a finite $\lambda > 0$, totally seven fixed points appear; three stable (O, $S_{1,2}$) and four unstable ones (U_{1-4}), as shown in Fig.7. As reaction proceeds, the
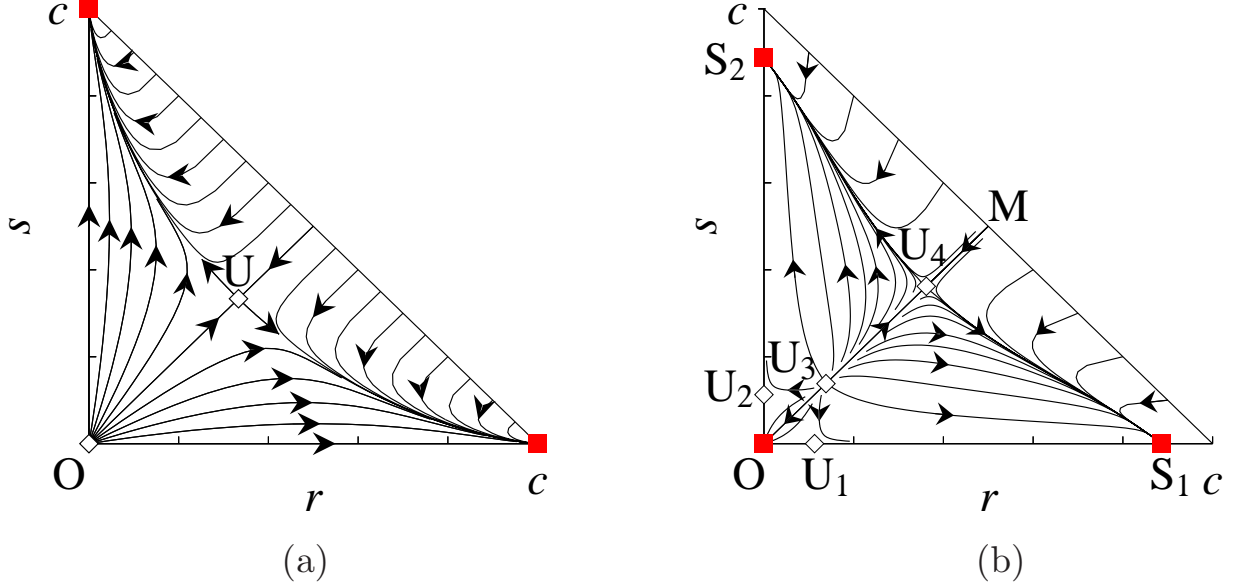
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FIG. 7: Flow diagrams with (a) a linear autocatalysis and a nonlinear recycling ($k_1 = \mu > 0$, $k_0 = k_2 = \lambda = 0$) similar to the Frank model, and (b) a quadratic autocatalysis and a linear recycling ($k_2 c^2 = \lambda > 0$, $k_0 = k_1 = \mu = 0$).

system approaches a state associated with one of the stable fixed points. The origin O is not interesting, since all the chiral products are recycled back to the achiral substrate. Also its influence extends only in a small region around O, bounded by U_{1-3}, if the life time $1/\lambda$ of chiral products is long enough. Close to this fixed point, influence of the spontaneous production process with k_0 should be taken into account, anyhow.

When the initial system is sufficiently away from O, the system approaches S_1 or S_2; Both correspond to homochiral states with $\phi_{1,\infty} = \pm 1$. When the initial configuration is close to the racemic state or the diagonal line $r = s$, the system approaches a racemic fixed point U_4 at first. But, while the recycling process returns the chiral enantiomers back to achiral substrate, the majority enantiomer increases its population at the cost of the minority one along the flow curve diverging from U_4 to S_1 or to S_2, and eventually the whole system becomes homochiral.

One may wonder whether recycling processes such as a linear or a nonlinear back reaction exist in relevant autocatalytic systems. So far, we are not aware of their existence. It is, however, possible that the back reaction rates λ or μ are nonzero but exceedingly small to be detected in laboratory experiments. Concerning with the problem of homochirality in

life, very small λ or μ are not unimaginable, considering the geological time scale for its establishment on earth.

On the other hand, a possibility to provide a system with a recycling process is proposed theoretically [26]: One simply let the reaction with ee amplification run in an open flow reactor. In an open system there is reactant flows between the system and the environment E. Let the solution with the achiral substrate A be supplied by an inflow with an influx F as

$$E \xrightarrow{F} A \tag{46}$$

and the products R and S as well as the substrate A be taken out by an outflow with a flow out rate λ as

$$A \xrightarrow{\lambda} E, \qquad R \xrightarrow{\lambda} E, \qquad S \xrightarrow{\lambda} E. \tag{47}$$
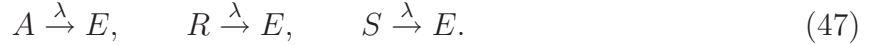
In terms of rate equations the processes are described as

$$\frac{dr}{dt} = f(r)a - \lambda r, \quad \frac{ds}{dt} = f(s)a - \lambda s,$$
$$\frac{da}{dt} = -[f(r) + f(s)]a + F - \lambda a. \tag{48}$$

Since the total concentration $a + r + s$ follows the time evolution $d(a + r + s)/dt = F - \lambda(a + r + s)$, it approaches the steady state value F/λ with a relaxation time $1/\lambda$. This is a consequence of unbiased outflow (48) of all reactants with the same rate λ. Consequently, even though we are dealing with an open system under a flow, the analysis is similar to the closed system by replacing the total concentration c with the steady state value F/λ. Instead of recycling, therefore, constant supply of the substrate allows the system to reach a certain fixed point with a definite value of the order parameter ϕ_1, independent of the initial condition.

VI. SUMMARY AND DISCUSSIONS

We have presented various simple scenarios that we are aware of in relevance to the ee amplification of the Soai reaction; a quadratic autocatalytic model in a monomer or a homodimer system, or a linear autocatalytic model in an antagonistic heterodimer system. All these models can realize ee amplification such that the final value of the ee $|\phi_\infty|$ depends

on but is larger than the initial value $|\phi_0|$, as schematically shown in Fig.8. The curve in the figure represents $\phi_0 - \phi_\infty$ relation for a given initial ratio q_0/c, namely the ratio of the amount q_0 of the total chiral initiators R and S relative to that of the total reactants c. Amplification is more enhanced if the ratio of the chiral initiator q_0/c is smaller. This plot also shows the possibility to increase the final ee by repeating the reaction.

To achieve high ee values, Soai et al. performed experiments of consecutive autocatalytic reactions, where after each run of the reactions, resulting solutions are quenched by adding acid and purified and reused in the next reactions. How the high ee value is attained in this type of experimental procedures can be explained illustratively in Fig.8. By choosing a specified initial condition $\phi_0^{(1)}$, the autocatalytic reaction ends up giving a final ee as $\phi = \phi_\infty^{(1)}$ determined by the intersection between the vertical line starting from $\phi_0^{(1)}$ point and the round curve. The consecutive reaction starts with the purified products with the ee $\phi_\infty^{(1)}$ as the initial ee $\phi_0^{(2)}$. This feature is illustrated by extending a horizontal line from $\phi_\infty^{(1)}$ on the round curve to the $\phi_0 = \phi_\infty$ straight slope. This second reaction yields the ee value $\phi_\infty^{(2)}$, which is determined by the intersection between the vertical line starting from $\phi_0^{(2)} = \phi_\infty^{(1)}$ point and the round curve. To repeat these procedures, the ee approaches rapidly the perfect $|\phi_\infty^{(\infty)}| = 1$ with the speed depending on the curvature of the curve, which is determined by q_0/c. This is a mechanism of ee amplification and consecutive autocatalytic reactions, in contrast with the chiral symmetry breaking in the sense of statistical mechanics, where the final ee is unique and is reached by a single procedure.

In all the cases considered, autocatalytic processes must be present, whether it be linear or nonlinear. To understand the actual mechanism of autocatalysis for the Soai reaction, the identification of the process at a molecular level is necessary, but that is out of scope of the present review.

We would like to point out another interesting feature, namely the spatial aspect of the reaction [24, 28, 36]. In usual experiments, the reactor is stirred to keep the system homogeneous. If there is no stirring, inhomogeneous patterns may develop between domains of two enantiomers. Analysis of these patterns may give some insight into the mechanism of reaction dynamics. Let us imagine, for instance, a time evolution of patterns of chiral domains for diffusionless systems with ee amplification and with a chiral symmetry breaking. In an initial stage chiral domains are nucleated randomly, and the domain pattern may look similar for both systems. After domains come in touch with each other, they behave dif-
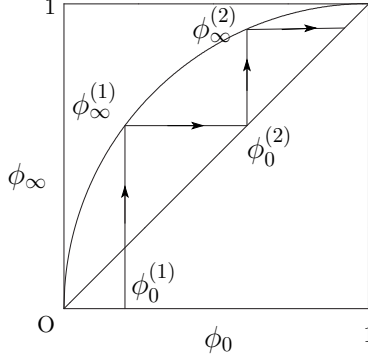
FIG. 8: Schematics of enantiomeric excess amplification.

ferently: For a system with ee amplification, domain pattern freezes because there remains no achiral substrate for further reactions. On the other hand, for a system with the chiral symmetry breaking, neighboring domains compete with each other at domain boundaries to extend their own territories, and the domain pattern evolves to selection slowly. When diffusion or hydrodynamic flow effects are taken into account, the system with ee amplification simply homogenizes and the ee value shall be averaged out. For the system with the chiral symmetry breaking, these transport processes speed up the chirality selection and enhance the final value of ee [28, 36].

So far we have discussed the ee amplification by starting from an initial state with a finite enantiomeric imbalance, and the effect of spontaneous reaction is mostly neglected, $k_0 = 0$. However, reaction experiments without adding chiral substances do produce chiral species [12, 13, 14], implying that the coefficient k_0 of the spontaneous reaction should be nonzero. In these experiments, it is found that values of the ee order parameter ϕ of many runs are distributed widely between -1 and $+1$, and the probability distribution function has double peaks at positive and negative values of ϕ.

There is a theoretical study on the asymptotic shape of probability distribution for nonautocatalytic and linearly autocatalytic systems with a specific initial condition of no chiral enantiomers [34, 35]. Even though no ee amplification is expected in these cases, the probability distribution with a linear autocatalysis has symmetric double peaks at $\phi = \pm 1$ when k_0 is far smaller than k_1; $k_0 \ll k_1/N$ with N being the total number of all reactive chemical species, A, R and S. This can be explained by the "single-mother" scenario for the realization of homochirality, as follows. From a completely achiral state, one of the chiral

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molecule, say R, is produced spontaneously and randomly after an average time $1/2k_0N$. Then, the second R is produced by the autocatalytic process whereas for the production of the first S molecule the spontaneous production is necessary. The waiting time for the second R is shorter than that for the first S by a factor about k_0/k_1. If this factor is far smaller than $1/N$, there is only a negligible chance for the production of S enantiomer until all the achiral substrates turn into R. All the chiral products are the descendants of the first mother R produced by the autocatalysis, and no second mother is born by the spontaneous production: This is a single-mother scenario. It strongly reflects the stochastic character of the chemical reaction, and is not contained in the average description using rate equations. Further studies are necessary as for the stochastic aspects of the Soai reaction [37].

In relation to the origin of homochirality in life, an interesting question is whether the ee amplification is sufficient to achieve homochirality. From the experimental results of the Soai reaction without chiral initiator, the magnitude of the final ee $|\phi_\infty|$ is distributed from a small value to a value close to unity. It is rather difficult to imagine that a value close to unity has been accidentally selected on various places on earth in the prebiotic era. It seems rather natural that chiral symmetry breaking took place and a unique value of $|\phi|$ has been finally selected. As has been discussed in the previous section, the flow in the open system can alter the system with ee amplification to the one with the chiral symmetry breaking. So we may say that the system with ee amplification in an open flow is one possibility. Recently, there appears several theoretical proposals such as polymerization models [26, 38, 39] or a polymerization-epimerization model [40] to realize the chirality selection in polymer synthesis. Although we are still far away from satisfactory understanding of the origin of homochirality in life, the discovery of the autocatalytic reaction by Soai gives us great impetus and a sense of reality to this problem.

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